EDITORIAL 10.1111/j.1469-0691.2008.01970.x

MRSA in livestock animals—an epidemic waiting to happen?

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ABSTRACT

Screening of pig farmers and pigs in The Netherlands has revealed that >20% of pig farmers and 39% of slaughterhouse pigs are positive for an unusual strain of methicillin-resistant *Staphylococcus aureus* (MRSA) belonging to sequence type (ST) 398. It is now clear that the emergence of ST398 is not just a Dutch problem, with human infections being described in several European countries, Canada and Singapore. Furthermore, some human isolates have now acquired the genes encoding Panton–Valentine leukocidin. Livestock may become an important source of community-acquired MRSA. A concerted effort on the part of clinicians, infection control practitioners and veterinarians will be required to prevent further spread of this novel strain of MRSA.

Keywords Community-acquired MRSA, epidemiology, livestock, methicillin-resistant *Staphylococcus aureus*, pig farming, ST398

Clin Microbiol Infect 2008; **14**: 519–521

During 2004, several cases of unexpected colonisation of individuals in direct or indirect contact with pigs with methicillin-resistant *Staphylococcus aureus* (MRSA) were described in The Netherlands [1]. Subsequent screening of pig farmers and pigs revealed that >20% of pig farmers and 39% of slaughterhouse pigs were MRSA-positive. These isolates were unusual in that they could not be typed by pulsed-field gel electrophoresis following *Sma*I digestion of chromosomal DNA, seemingly because of an as yet unknown change in the methylation system [2]. A recent retrospective case-control analysis revealed a strong association of MRSA carriage and contact with either pigs or veal calves [3]. The MRSA isolates of animal origin all belonged to a number of closely related spa types (t011, t108, t567), which corresponded to multilocus sequence type (ST) 398, a hitherto unusual type in humans. While a single non-typeable (NT) MRSA isolate from 1998 was described in a French study [4], no further reports concerning this MRSA strain appeared between 1998 and 2003. However, in countries in which MRSA is highly endemic (e.g., France), the association between animal contact and MRSA colonisation/infection may have been overlooked.

The process by which this strain emerged in the animal population and subsequently in humans is unclear. ST398 might originally have been a highly prevalent pig strain of methicillin-susceptible *S. aureus* that then acquired *mecA* from other staphylococci that colonise pigs or pig farmers. The fact that several different SSC*mec* elements have been found in MRSA ST398 suggests that this event must have occurred on several occasions [5]. While some believe that the (over)use and consequent high selective pressure of antibiotics, e.g., tetracyclines, in the pig population is an important contributor to the problem, others consider that the international trade in pigs, e.g., between high- and low-prevalence MRSA countries, contributed to the emergence of ST398. Part of the reason for the rapidly increasing use of antibiotics/occurrence of ST398 MRSA could be related to the ban on avoparcine use. The coexistence of an extensive network of pig farms in a relatively small country may have facilitated the spread of ST398 within The Netherlands. It is now

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a fact that MRSA can be found at all levels of the pig-breeding chain in The Netherlands [6].

It has become clear in the past year that the emergence of ST398 strains in humans is not just a Dutch problem. MRSA strains of this type have been isolated from professionals in contact with pigs in several other European countries, e.g., Belgium, Germany, Italy, Spain and Denmark, as well as in Canada and Singapore [7]. While the spread to other European countries could be facilitated by the extensive transport of livestock among these countries, this is not usually the case between continents.

It has been suggested that MRSA ST398 has a limited capacity for inter-human spread and is less (if at all) virulent. However, when considering the epidemiology of these strains, it should be remembered that ST398 has been followed for 4–5 years, whereas experience with 'classic MRSA' strains now exceeds 40 years. Furthermore, the epidemiology of ST398 appears to be different from that of classic MRSA strains, which emerged mainly in hospitals, among patients with severe underlying disease. When the first MRSA strains were isolated, several investigators thought that these strains would be of limited clinical interest. However, 25 years later (in 1988), the first Dutch MRSA control guidelines were implemented in response to the, by then, worldwide MRSA epidemic. Therefore, any assumptions concerning the ability of MRSA ST398 to spread or cause clinical infections should be postponed until further data are available.

In The Netherlands, Germany and Denmark, community-acquired and hospital-acquired MRSA ST398 infections in humans have been described, including endocarditis [8], ventilator-associated pneumonia [9] and wound infections [10] (R. Skov, personal communication). Although the strains isolated from pigs have all been Panton–Valentine leukocidin-negative, some human isolates have been shown to harbour the genes encoding production of Panton–Valentine leukocidin, thereby illustrating the capacity of MRSA ST398 to pick up additional virulence factors. Transmission among family members and from patients to healthcare workers has been demonstrated. Knowing that inter-human spread is possible, it is probably just a matter of time before the first outbreak involving ST398 occurs. It is currently too soon to predict how epidemic this strain will become in the hospital environment. Individuals in contact with pigs and veal calves are at risk of becoming colonised with MRSA, and consequently of developing MRSA infections. When 25–50% of a certain profession (e.g., pig farmers) are shown to carry MRSA, a different approach to empirical antibiotic therapy of serious staphylococcal infections in members of this profession is demanded.

Zoonotic MRSA will have a major impact on countries that apply a search-and-destroy strategy to control MRSA. In The Netherlands, an active screening policy for individuals in contact with pigs and veal calves has resulted in a steep increase in the number of MRSA-positive patients, with a subsequent increase in the associated workload and costs, especially in hospitals with rural catchment areas [11]. The proportion of NT MRSA reported to the national reference centre has increased from 0% before 2003 to account for 33% of all reported cases of MRSA during the first half of 2007. The challenge is not only to deal with the sheer number of patients who need screening and isolation, but also the fact that it is almost impossible to apply the 'destroy' part of the MRSA control strategy, since patients with constant exposure to MRSA in their work and home settings cannot be decolonised. Professionals in contact with livestock have an increased chance of becoming colonised with NT MRSA, which is a type of MRSA that is here to stay and that will accompany them in all their contacts within the healthcare system. Since instigating isolation precautions can have detrimental effects on care for the individual patient, this raises some difficult medical–ethical dilemmas.

An important part of a solution to this new dilemma would be to tackle the problem at its source, namely the livestock animals. Since the majority of ST398 MRSA isolates are tetracycline-resistant, and oxytetracyclines are the antibiotics used most frequently in pig farming, revisiting policies for the use of antibiotics in livestock is necessary. In the case of severe epidemics with, e.g., highly pathogenic avian influenza, foot and mouth disease and classic swine fever, it has been possible to control epidemics in livestock efficiently. In such cases, the driving force has been the economic consequences of the epidemic. In the case of ST398 MRSA, healthcare consequences should elicit the same or an even higher priority.

In conclusion, livestock may become an important reservoir and source of community-acquired

MRSA. The use of antibiotics in farming not only selects for the occurrence of MRSA ST398, but also carries the risk that such strains will become truly multiresistant. Whether MRSA ST398 is here to stay within the human population remains to be seen, but it has already shown the potential to both colonise and infect humans. Additional insight is needed into the transmission routes between animals and their carers in order to find ways of controlling transmission. A concerted effort on the part of clinicians, infection control practitioners and veterinarians is needed to prevent further spread of this novel strain of MRSA.

ACKNOWLEDGEMENTS

The authors declare that no conflicts of interest exist in relation to this article.

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